

WHAT IS CLAIMED IS:

1. A process for preparing (3S,4S)-N-((1S,4S)-4-isopropyl-4-{[3-(trifluoromethyl)-7,8-dihydro-1,6-naphthyridin-6(5H)-yl]carbonyl}cyclopent-2-en-1-yl)-3-methoxytetrahydro-2H-pyran-4-amine comprising the steps of:

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(1) reacting (1S,4S)-4-(2,5-dimethyl-1H-pyrrol-1-yl)-1-isopropylcyclopent-2-ene-1-carboxylic acid with 3-(trifluoromethyl)-5,6,7,8-tetrahydro-1,6-naphthyridine;

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(2) treating 6-{[(1S,4S)-4-(2,5-dimethyl-1H-pyrrol-1-yl)-1-isopropylcyclopent-2-en-1-yl]carbonyl}-3-(trifluoromethyl)-5,6,7,8-tetrahydro-1,6-naphthyridine with hydroxylamine; and

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(3) coupling (1S,4S)-4-isopropyl-4-{[3-(trifluoromethyl)-7,8-dihydro-1,6-naphthyridin-6(5H)-yl]carbonyl}cyclopent-2-en-1-amine with (3R)-3-methoxytetrahydro-4H-pyran-4-one.

2. A process for the preparing ((1R,3S)-3-isopropyl-3-{[3-(trifluoromethyl)-7,8-dihydro-1,6-naphthyridin-6(5H)-yl]carbonyl}cyclopentyl)[(3S,4S)-3-methoxytetrahydro-2H-pyran-4-yl]amine comprising the steps of:

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(1) reacting (1S,4S)-4-(2,5-dimethyl-1H-pyrrol-1-yl)-1-isopropylcyclopent-2-ene-1-carboxylic acid with 3-(trifluoromethyl)-5,6,7,8-tetrahydronaphthyridine;

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(2) treating 6-{[(1S,4S)-4-(2,5-dimethyl-1H-pyrrol-1-yl)-1-isopropylcyclopent-2-en-1-yl]carbonyl}-3-(trifluoromethyl)-5,6,7,8-tetrahydro-1,6-naphthyridine with hydroxylamine;

(3) coupling (1S,4S)-4-isopropyl-4-{[3-(trifluoromethyl)-7,8-dihydro-1,6-naphthyridin-6(5H)-yl]carbonyl}cyclopent-2-en-1-amine with (3R)-3-methoxytetrahydro-4H-pyran-4-one; and,

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(4) hydrogenating (3S,4S)-N-((1S,4S)-4-isopropyl-4-{[3-(trifluoromethyl)-7,8-dihydro-1,6-naphthyridin-6(5H)-yl]carbonyl}cyclopent-2-en-1-yl)-3-methoxytetrahydro-2H-pyran-4-amine.

3. A process for preparing ((1R,3S)-3-isopropyl-3-{{3-(trifluoromethyl)-7,8-dihydro-1,6-naphthyridin-6(5H)-yl}carbonyl}cyclopentyl)[(3S,4S)-3-methoxytetrahydro-2H-pyran-4-yl]amine succinate comprising the steps of:

5 (1) reacting (1S,4S)-4-(2,5-dimethyl-1H-pyrrol-1-yl)-1-isopropylcyclopent-2-ene-1-carboxylic acid with 3-(trifluoromethyl)-5,6,7,8-tetrahydronaphthyridine;

(2) treating 6-{{[(1S,4S)-4-(2,5-dimethyl-1H-pyrrol-1-yl)-1-isopropylcyclopent-2-en-1-yl]carbonyl}-3-(trifluoromethyl)-5,6,7,8-tetrahydro-1,6-naphthyridine with hydroxylamine;

10 (3) coupling (1S,4S)-4-isopropyl-4-{{3-(trifluoromethyl)-7,8-dihydro-1,6-naphthyridin-6(5H)-yl}carbonyl}cyclopent-2-en-1-amine with (3R)-3-methoxytetrahydro-4H-pyran-4-one; and,

15 (4) hydrogenating (3S,4S)-N-((1S,4S)-4-isopropyl-4-{{3-(trifluoromethyl)-7,8-dihydro-1,6-naphthyridin-6(5H)-yl}carbonyl}cyclopent-2-en-1-yl)-3-methoxytetrahydro-2H-pyran-4-amine.

20 (5) contacting ((1R,3S)-3-isopropyl-3-{{3-(trifluoromethyl)-7,8-dihydro-1,6-naphthyridin-6(5H)-yl}carbonyl}cyclopentyl)[(3S,4S)-3-methoxytetrahydro-2H-pyran-4-yl]amine with succinic acid.

4. A process for preparing (1S,4S)-4-(2,5-dimethyl-1H-pyrrol-1-yl)-1-isopropylcyclopent-2-ene-1-carboxylic acid comprising the steps of:

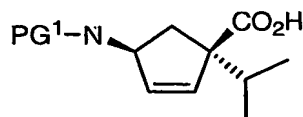
25 (1) reacting (1R,4S)-4-aminocyclopenten-2-ene-1-carboxylic acid with MeOH and thionyl chloride;

30 (2) reacting methyl (1R,4S)-4-aminocyclopenten-2-ene-1-carboxylate with acetylacetone;

(3) reacting methyl (1R,4S)-4-(2,5-dimethyl-1H-pyrrol-1-yl)cyclopent-2-ene-1-carboxylate with 2-iodopropane; and,

(4) reacting methyl (1S,4S)-4-(2,5-dimethyl-1H-pyrrol-1-yl)-1-isopropylcyclopent-2-ene-1-carboxylate with NaOH and MeOH.

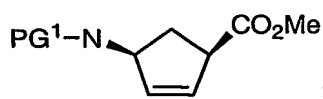
5 5. A process for the preparing:



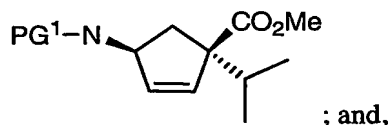
comprising the steps of:

10 (1) reacting (1R,4S)-4-aminocyclopenten-2-ene-1-carboxylic acid with MeOH and thionyl chloride;

15 (2) adding a protecting group (P.G.¹) to the product of (1) to form:



(3) reacting the product of step (2) with 2-iodopropane to form:



; and,

20 (4) reacting the product of step (3) with NaOH and MeOH.

6. The process of claim 5 wherein the protecting group is selected from: *tert*-butoxycarbonyl, benzyloxycarbonyl, alkyloxycarbonyl, allyloxycarbonyl, benzoyl, formyl, trifluoroacetyl, acetyl, 2-nitrobenzenesulfonyl, 4-nitrobenzenesulfonyl, 2,4-dinitrobenzenesulfonyl, benzyl, triphenylmethyl, and various imines (including diphenylmethyleimine).

7. A process for preparing 3-(trifluoromethyl)-5,6,7,8-tetrahydro-1,6-naphthyridine comprising the steps of:

- (1) reacting 3,3,3-trifluoropropionic acid with POCl₃, DMF, NaPF₆ and a base;
- (2) reacting CF₃DT with a protected piperidone; and
- (3) reacting N-(protecting group)-3-(trifluoromethyl)-5,6,7,8-tetrahydronaphthyridinene in the presence of HCl and methanol.

8. The process of claim 7 wherein the protecting group is selected from: *tert*-butoxycarbonyl, benzyloxycarbonyl, alkyloxycarbonyl, allyloxycarbonyl, 2-nitrobenzenesulfonyl, 4-nitrobenzenesulfonyl, 2,4-dinitrobenzenesulfonyl, benzoyl, acetyl, formyl, trifluoroacetyl, N-benzyl, and triphenylmethyl.

9. The process of claim 7 wherein the protecting group is *tert*-butoxycarbonyl (BOC).

10. A process for the preparing (3R)-3-methoxytetrahydro-4H-pyran-4-one comprising the steps of:

- (1) reacting tetrahydro-4H-pyran-4-one with tripropylorthoformate and chlorobenzene;
- (2) reacting 4-propoxytetrahydro-2H-pyran-ethene in the presence of acetone, water, hydroquinidine-1,4-phthalazinediyl diether (DHQD₂PHAI), potassium osmate dehydrate, and 4-methylmorpholine N-oxide monohydrate (NMO);
- (3) reacting 3,4-dihydroxy-tetrahydro-2-H-pyran-4-sulfonic acid, sodium salt with methanol and trimethylorthoformate in the presence of an acid; and
- (4) reacting 4,4-dimethoxytetrahydro-2H-pyran-3-ol in the presence of THF, NaOt-Bu, Me₂SO₄, and an acid.